

REMARKS

This Amendment cancels claim 32 and amends claim 23. Page 5, lines 31-33 support the dissolution-controlled release feature of claim 23. Claims 23-31 are pending.

Examiner Tran is thanked for indicating claims 29 and 30 would be allowable if rewritten in independent form to include all the limitations of the base claim and any intervening claims. It is believed this Amendment places the entire application in condition for allowance for the reasons set forth below.

The 35 U.S.C. § 103(a) rejection of claims 23-28, 31 and 32 over U.S. Patent No. 5,591,453 to Ducheyne et al. in view of PCT Patent Publication WO 92/20623 to Einarsrud et al. is respectfully traversed. A feature of method claim 23 is the use of a delivery device which comprises a controllably dissolvable silica-xerogel which contains a biologically active agent. A second feature of the claimed method is that release of the biologically active agent at a substantially constant rate from the silica-xerogel is based on complete dissolution of the silica-xerogel matrix.

The cited combination of references fails to raise a prima facie case of obviousness against the claimed method because neither reference suggests these features of the claimed methods.

First, Ducheyne et al. does not disclose a substantially constant rate of release from its matrix. Instead, Ducheyne et al. concedes the release kinetics of the biologically active molecules in the early stages of immersion is "higher than in the later stages," and suggests in vitro immersion to address the higher, early release before in vivo use in a patient if a steady state release is desired (Col. 15, lines 1-15).

Second, Ducheyne et al. fails to disclose or suggest complete dissolution of its silica-based matrix. None of its Examples indicate that its silica glass carriers completely dissolve when in contact with simulated body fluid.

One of ordinary skill in the art would understand the Ducheyne et al. carrier does not have to dissolve completely to achieve release of its biologically active agent. Ducheyne et al. teaches that a biologically active agent may be controllably released primarily by diffusion through the pores of its silica-based glass. See, for example, Col. 6, lines 15-17 ("In the case of pure silica glass, the release of the biological molecules from the carrier is effected primarily by diffusion through the pore structure"), Col. 9, lines 16-18 ("Because of the controllable microporosity, a subsequent controlled release of molecule is achieved."), and Col.

14, lines 38-39 ("Larger pore sizes facilitate the release of larger molecules through diffusion."). Since the primary release mechanism is taught to be diffusion, dissolution of the carrier is not required for release.

A Declaration Pursuant to 37 C.F.R. § 1.132 is attached in response to the Patent Office invitation to show Ducheyne et al.'s silica-glass matrix does not release its active agent by matrix dissolution. Unfortunately, the data presented by Ducheyne et al. do not provide definitive proof of the mechanism(s) governing release of the biologically active agent from the its matrix due to the methodology employed. Nevertheless, the Ducheyne et al. figures do not show or suggest that a biologically active agent contained in the Ducheyne et al. silica-xerogel is released at a substantially constant rate by complete dissolution of the silica-xerogel over a desired time period when in contact with body fluid.

The claimed method is thus patentable even if, arguendo, one or more of the Ducheyne et al. composites released its biologically active agent at least partially by a matrix dissolution mechanism, because there is no showing that complete dissolution occurs during release. See paragraph No. 33 of the Declaration.

Moreover, one of ordinary skill in the art is given no disclosure or suggestion that complete dissolution of the matrix occurs during release of its biologically active agent. As discussed above, Ducheyne et al. repeatedly mentions diffusion as the primary release mechanism; its single reference to matrix dissolution is made in the context of greater porosity of the matrix, with the comment that larger pores in the matrix facilitate the release of larger molecules through diffusion. See Col. 14, lines 34-37 of Ducheyne et al.

It is improper to use hindsight to provide disclosure missing the reference. In this case, there is no "complete dissolution" disclosure in Ducheyne et al. - even a very thorough review by an expert merely concludes that one or a few of Ducheyne et al.'s examples *may* have released biologically active agent by dissolution; there is no evidence of complete dissolution of the Ducheyne et al. matrix.

The deficiencies of Ducheyne et al. are not remedied by Einarsrud et al., which discloses high porosity gels suitable for window insulation. It is respectfully submitted Einarsrud et al. is from a non-analogous art. Even assuming, arguendo, these references are properly combined, their combination does not

disclose or suggest complete dissolution of a silica xerogel to permit controlled release at a substantially constant rate of a biologically active agent contained therein. Einarsrud et al. employs its silica xerogel as a building material; one of ordinary skill in the art would hardly intend for it to dissolve, much less at a constant rate. Finally, the degree of porosity of a silica-xerogel is not a key factor governing the dissolution of the gel in simulated body fluid. See Viitala et al., "Adjustably Bioresorbable Sol-Gel Derived SiO₂ Matrices for Release of Large Biologically Active Molecules," 36 J. Sol-Gel Sci. Tech. 147-156 (2005), which was previously submitted to the Office as part of the Request for Reconsideration filed September 1, 2006.

Reconsideration and withdrawal of the obviousness rejection of claims 23-28, 31 and 32 over Ducheyne et al. in view Einarsrud et al. are earnestly requested.

It is believed this application is in condition for allowance. Accordingly, withdrawal of the sole rejection of claims 23-28, 31 and 32, and issuance of a Notice of Allowance directed to claims 23-31, are earnestly requested. The Examiner is urged to telephone the undersigned should she believe any further action is required for allowance.

U.S. Appln. S.N. 10/828,351
AMENDMENT

PATENT

A Petition and fee for a two month Extension of Time are attached. It is not believed any fee is required for entry and consideration of this Amendment. Nevertheless, the Commissioner is authorized to charge our Deposit Account No. 50-1258 in the amount of any such required fee.

Respectfully submitted,

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Enclosures:

Petition for Extension of Time
Declaration Pursuant to 37 C.F.R. § 1.132